REMARKS

Entry of the foregoing and further and favorable reconsideration of the subject application, as amended, pursuant to and consistent with 37 C.F.R. § 1.112, and in the light of the remarks which follow, are respectfully requested.

By the present amendment, claim 1 has been amended. Support for the amendment to claim 1 can be found throughout the specification, e.g. at least in claim 2 as originally filed. New claims 39-42 have been added. Support for the added claims may be found in the specification at least on page 23 lines 3 to 15 as well as in Example 4 on page 47. No new matter has been added.

Turning now to the Official Action, Applicants would first like to point out that claims 25 and 26 appear to have been mistakenly incorporated into Group IV. Since these claims are dependent upon claim 22, Applicants submit that they should also be classified in Group II, which has now been rejoined. It is respectfully requested that these claims be considered together with the elected claims of Group I and II, particularly since no new issues are raised by these claims.

Applicants further note that the claims of Group II were characterized in the Official Action of July 21, 2000 as being drawn to a method of reducing phenotypic expression in a host cell by transformation with DNA encoding hairpin RNA and transformed host cell. Accordingly, it appears that claim 23, drawn to a host cell comprising hairpin RNA, has been mistakenly incorporated in Group II. Accordingly claim 23 should be withdrawn from consideration in the current application so that it may be considered with the other claims of group III.

Claim 22 has been objected to since it consisted of two sentences. Claim 22 has been amended to correct this deficiency.

Claim 22 is rejected under 35 U.S.C. § §112 as purportedly indefinite. This rejection, to

the extent that it applies to the claim as amended, is respectfully traversed.

At page 3 of the Official Action, the Examiner argues that claim 22, drawn to a composition, is indefinite in its recitation of a method step in the last two lines of the claim. Applicants respectfully submit that inclusion of process claims in a product, thus creating a "product- by-process" claim, is perfectly permissible, Nevertheless, without conceding to the Examiner's arguments, as noted above claim 22 has been amended to remove the method step, thus rendering this rejection moot.

Claims 1, 11 and 12 are also rejected under 35 U.S.C. §112, second paragraph as purportedly indefinite. This rejection, to the extent that it applies to the claims as amended, is respectfully traversed.

The Examiner, at page 4 of the Official Action, argues that claim 1 is indefinite in its recitation of "essentially similar to at least part", while claims 11 and 12 are rejected due to their dependency on claim 1.

"Essentially similar" with respect to nucleotide sequences has been defined in the specification at least on page 15 lines 17 to 23 as sequences having a sequence identity of at least about 75%. The notion "sequence identity" has been defined by a single definition (including the parameters required for the alignment of the nucleotide sequences), at least on page 15 lines 9 to 17. One skilled in the art would thus be perfectly capable of assessing whether a particular nucleotide sequence to be used for a particular nucleic acid of interest would fall within the scope of the claim or not.

In addition, by the present amendment, claim 11 has been amended to be dependent from claim 2, rather than from claim 1. This amendment should obviate this rejection as it applies to claims 11 and 12.

In view of the foregoing, Applicants submit that the present claims fully comply with the requirements of 35 U.S.C. § §112. Withdrawal of this rejection is thus respectfully requested.

Claims 1, 2, 3, 7, 8, 11, 12 , 22 and 23 are rejected under 35 U.S.C. § 102(b) as purportedly anticipated by Metzlaff *et al.*. This rejection, to the extent that it applies to the claims as amended, is respectfully traversed.

In making this rejection, the Examiner has represented Metzlaff et al. as disclosing a method wherein a foreign transgene, *chs*A has been introduced into petunia plants under control of the 35S promoter from cauliflower mosaic virus whereby the construct produces an RNA molecule comprising a region of 43 bp with 80% homology with chsA coding and 3' UTR and capable of forming a hairpin structure, and whereby the expression of this RNA can result in a phenotypic color change.

However, in the present case, each of the independent claims 1, 2, 22 and 23 explicitly state that the hairpin structure is **artificial**. An artificial hairpin RNA structure has been defined at least on page 22 of the specification, lines 19 to 28 as being

- a hairpin RNA not naturally occurring in nature because sense and antisense regions as defined are not naturally occurring simultaneously in one RNA molecule; or
- the sense and antisense regions are separated by spacer region which is heterologous; or
- the hairpin is not comprised within the RNA molecule it is normally associated with.

While it may be true that the chsA transgene introduced into the petunia plants also produces an RNA molecule comprising the same putative secondary structure with the 43bp hairpin structure represented in figure 5 and mentioned on page 851 for the RNA produced from the **endogenous** chsA gene, this does not qualify to make the hairpin structure artificial within the provided definitions.

The "sense" and "antisense" regions of the 43 bp stem of the hairpin structure are indeed naturally occurring in the chsA transcript of the endogenous chsA gene. Further, the "spacer region" making the loop is homologous, since its nucleotide sequence is identical to the chsA nucleotide sequence. Finally, the hairpin is comprised within the RNA molecule (the chsA transcript) with which it is normally associated. In other words, the hairpin structure does not comply with any of the provided definitions for an "artificial hairpin structure".

Thus, the method disclosed by Metzlaff does not meet all the features of the claimed methods as required by 35 U.S.C. § §102, and thus cannot anticipate claims 1, 2, 3, 7, 8, 11, 12, 22 and 23. Withdrawal of the rejection is respectfully requested.

Claims 1 to 6, 9 to 12, 22 and 23 are rejected under 35 U.S.C. § §102(b) as purportedly anticipated by Agrawal et al. This rejection, to the extent that it applies to the claims as amended, is respectfully traversed.

The Examiner argues, at page 5 of the Official Action, that Agrawal et al. disclose methods for reducing the expression of a gene using an antisense oligonucleotide which comprises a self complementary region and wherein the self complementary region comprises at least 10 complementary nucleotides and wherein the self complementary region is complementary to a target gene.

However, in the present case, independent claims 1, 2 and 22 recite methods comprising the step of introduction of a chimeric DNA comprising an operative promoter and a transcribed DNA region which when transcribed yields the RNA molecule comprising the artificial hairpin RNA structure. In contrast, Agrawal et al disclose a method for inhibiting the gene expression of a virus, a pathogenic organism or a cellular gene comprising the step of providing directly the self-stabilized oligonucleotides or ribozymes as defined therein, to cells (page 17 last paragraph).

The only methods disclosed for providing such self-stabilized oligonucleotides are administering the oligonucleotides, preferably via the oral, intranasal, rectal or topical route (page 18, lines 5 to 10). Nowhere in the document has it even been suggested that the self stabilized oligonucleotides are provided to the cells by introduction of a **chimeric DNA** comprising a **promoter** and a DNA region which when transcribed would yield an RNA molecule with an artificial hairpin RNA structure.

Thus, the methods disclosed by Agrawal et al. do not meet all the features of the claimed methods and cannot anticipate claims 1 to 6, 9 to 12, 22. In view of the above, withdrawal of the rejection is respectfully requested.

From the foregoing, favorable action in the form of a Notice of Allowance is respectfully requested and such action is earnestly solicited.

In the event that there are any questions concerning this paper, or the application in general, the Examiner is respectfully urged to telephone the undersigned so that prosecution of the application may be expedited.

Respectfully submitted,

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Attachment to Reply dated August 24, 2001

Marked-up Claims - 1, 11 and 22

1. (Twice Amended) A method for reducing the phenotypic expression of a nucleic acid of interest, which is normally capable of being expressed in a eucaryotic cell, comprising the step of introducing a chimeric DNA comprising the following operably linked parts:

a) a promoter, operative in said eucaryotic cell;

b) a DNA region, which when transcribed, yields an RNA molecule comprising an RNA region capable of forming an artificial hairpin RNA structure, wherein one of the annealing RNA sequences of the hairpin RNA structure comprises a sequence, essentially similar to [at least] a part of at least 10 consecutive nucleotides of the nucleotide sequence of said nucleic acid of interest, and wherein the second of said annealing RNA sequences comprises a sequence essentially similar to [at least] a part of at least 10 consecutive nucleotides of the complement of at least part of said nucleotide sequence of said nucleic acid of interest; and optionally

c) a DNA region involved in transcription termination and polyadenylation.

11. (Amended) The method according to claim [1] 2, wherein said eucaryotic cell is a plant cell.

22. (Amended) A eucaryotic cell, comprising a nucleic acid of interest, which is normally capable of being phenotypically expressed, further comprising a chimeric DNA molecule comprising the following operably linked parts:

a) a promoter, operative in said eucaryotic cell;

b) a DNA region, which when transcribed, yields an RNA molecule with at least one RNA region with a nucleotide sequence comprising

i. a sense nucleotide sequence of at least 10 consecutive nucleotides having between 75 and 100% sequence identity with at least part of the nucleotide sequence of the nucleic acid of interest; and

ii. an antisense nucleotide sequence including at least 10 consecutive nucleotides, having between about 75% to about 100% sequence identity with the complement of said at least 10 consecutive nucleotides of said sense nucleotide sequence;

wherein the RNA is capable of forming an artificial hairpin RNA structure with a double stranded RNA stem by base-pairing between the regions with sense and antisense nucleotide sequence; and optionally

c) a DNA region involved in transcription termination and polyadenylation.

[wherein the phenotypic expression of said nucleic acid of interest is significantly reduced.]